


## Original Article

# Acute metaldehyde poisoning from ingestion: clinical features and implications for early treatment

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**Aims:** To describe and compare the clinical features of patients with acute metaldehyde toxicity from suicidal and accidental ingestion of metaldehyde, and to elucidate factors influencing early treatment and disposition.

**Methods:** We undertook a systematic review and retrospective analysis of the clinical characteristics and outcomes of patients with acute toxicity from ingesting metaldehyde.

**Results:** Twenty-one cases identified between 1965 and 2021 were analyzed. The median age was 32 years (range, 3–68 years), and two-thirds of patients experienced symptoms (14/21, 67%). In symptomatic patients, gastrointestinal symptoms were present in two-thirds (9/14, 64%), and half experienced neurologic complications (8/14, 57%); of those with neurologic complications, half experienced seizures (8/14, 57%). There were near-equal cases of accidental and suicidal poisoning. Those who attempted suicide were likelier to develop symptoms (90% versus 45%,  $P = 0.031$ ), experience seizures (60% versus 18%,  $P = 0.049$ ), require intensive care (50% versus 9%,  $P = 0.038$ ), and suffer longer hospitalizations (13.3 days versus 2.9 days,  $P = 0.005$ ), despite no statistically significant differences in the doses of metaldehyde consumed when compared against patients with accidental ingestion (9.04 g versus 2.03 g,  $P = 0.09$ ).

**Conclusion:** The circumstances in which metaldehyde is consumed heavily influence clinical symptoms and outcomes. Early and close observation for seizures and adopting a lowered threshold for escalation to the intensive care unit are recommended in patients attempting suicide even when the dose ingested cannot be determined at that time, which is common during the early phases of treatment.

**Key words:** Metaldehyde, poisoning, suicide, toxicity, toxicology

## INTRODUCTION

METALDEHYDE IS A popular and potent molluscicide commonly used against slugs and snails.<sup>1,2</sup> Toxic when ingested, it is readily absorbed in the gastrointestinal tract, causing a myriad of multisystemic complications. Despite its widespread use, reports of acute toxicity in humans are exceedingly rare when compared to other mammals. Consequently, there are significant gaps in our knowledge of the clinical features and outcomes of acute metaldehyde toxicity in humans.<sup>1</sup> Additionally, early

estimation of ingested metaldehyde dose is frequently difficult due to incomplete clinical history and circumstantial evidence during the initial phases of treatment. Point-of-care testing for blood metaldehyde level is often unavailable, rendering it difficult for the treating physicians to decide on the initial management and disposition of these patients. Therefore, we undertook a systematic review of relevant published reports over the past 65 years, so as to better describe the clinical characteristics of acute toxicity in humans from suicidal and accidental ingestion of metaldehyde, and to elucidate factors that influence the initial management and disposition of these patients.

## METHODS

WE CARRIED OUT a search on PubMed and Google Scholar for relevant reports over the past 65 years (1956–2021) using the keywords “metaldehyde,” “molluscicide,” “metaldehyde poisoning,” “humans,” and

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Received 22 Feb, 2022; accepted 20 May, 2022

### Funding information

No funding information provided.

“metaldehyde toxicity.” Articles in languages other than English, or involved toxicity in nonhumans, were duly excluded. Patients exposed to metaldehyde from other mechanisms other than ingestion, or with concurrent ingestion of multiple co-ingestants, or without adequate descriptions of clinical features, were omitted from our study. The clinical features of identified cases were retrospectively analyzed, after which statistical analysis was carried out using the Mann–Whitey *U*-test, unpaired *t*-test, Pearson’s  $\chi^2$ -test, and Fisher’s exact test as appropriate with a two-tailed alpha of 0.05.

## RESULTS

**W**E IDENTIFIED a total of nine relevant articles on metaldehyde poisoning in humans between 1956 and 2021. One study was omitted due to the presence of multiple co-ingestants at significant doses. Excluding a patient who developed metaldehyde toxicity through dermal exposure, a total of 21 patients were retrospectively analyzed, and their demographic profile, clinical features, and eventual outcomes are summarized in Table 1.<sup>2–9</sup> The median age was 32 years (range, 3–68 years). There were slightly more male than female patients (12 male patients, 9 female patients). Eleven patients (11/21, 52%) ingested metaldehyde accidentally, whereas the remaining 10 (10/21, 48%) did so while attempting suicide. Among the eight patients with their past medical histories available for analysis, seven (7/8, 88%) had pre-existing psychiatric disorders, of which depression was the most common (5/7, 71%). Mental retardation with pica and schizophrenia were present in Patients 18 and 21, respectively.

### Clinical features and outcomes

Two-thirds of the patients (14/21, 67%) developed symptoms, of which gastrointestinal (9/14, 64%) and neurologic manifestations (8/14, 67%) preponderated. Nausea, vomiting, and/or diarrhea were the most common gastrointestinal symptom (7/9, 78%). Among those patients with neurologic symptoms, at least half developed seizures (8/14, 57%). Less common neurologic features included facial dystonia (patient 17), poorly reactive pupils (patients 1 and 3), and brachial plexopathy (Patient 21). Rhabdomyolysis was described in three, occurring with concomitant seizures in Patients 2 and 3. Tachycardia and blood pressure derangements were rare. Patient 1 was tachycardic and hypertensive, whereas Patients 3 and 17 were tachycardic but hypotensive. Patient 7 experienced only tachycardia without perturbations of blood pressure. Pyrexia (3/21, 14%; Patients 1, 3, and 17) and diaphoresis (3/21, 14%, Patients 2, 3, and 19) were also

uncommon. Acid–base derangements were comparatively frequent, and were present in nearly a quarter of patients (5/21, 24%), among whom Patients 3, 17, and 21 had high anion gap metabolic acidosis (HAGMA).

The doses of ingested metaldehyde were varying and incompletely reported across these studies, either as absolute amounts (g) or as a proportion to the patient’s weight (mg/kg). The absolute doses of consumed metaldehyde were reported in 12 patients, with an average dose of 4.95 g (range, 0.5–18.9 g) ingested. The serum metaldehyde level was measured only in Patient 18, revealing a concentration of 80.6  $\mu\text{g/mL}$ . Regardless, deaths were uncommon (2/21, 10%), and early recovery within 1 week occurred in nearly three-quarters of cases (15/21, 71%). Patient 18 died from respiratory failure secondary to acute lung injury, but the cause of death was left unspecified in Patient 3. Understandably, patients who experienced recovery within 1 week tended to be younger (17 years versus 42.5 years,  $P = 0.008$ ), had accidental rather than suicidal ingestion of metaldehyde (83% versus 33%,  $P = 0.038$ ), and ingested metaldehyde at much lower doses (2.25 g versus 10.35 g,  $P = 0.021$ ).

### Comparison of suicidal and accidental ingestion of metaldehyde

The average dose of metaldehyde consumed tended to be higher in suicidal than in accidental ingestion (9.04 g versus 2.03 g,  $P = 0.09$ ) (Table 2). However, this finding did not achieve statistical significance, likely due to the variable and incomplete manner in which the doses were reported in the analyzed studies. Patients with suicidal ingestion of metaldehyde were older than those with accidental ingestion (median age, 39 years versus 6 years,  $P = 0.009$ ) and tended to develop symptomatic toxicity (90% versus 45%,  $P = 0.0305$ ). They were also three times likelier to experience seizures (60% versus 18%,  $P = 0.049$ ). Understandably, they were five times likelier to require admissions to the intensive care unit (ICU; 50% versus 9%,  $P = 0.038$ ), and their hospitalizations were more than four times longer than those with accidental ingestion of metaldehyde (13.3 days versus 2.9 days,  $P = 0.005$ ).

## DISCUSSION

**C**ASES OF ACUTE toxicity in humans from ingesting metaldehyde were uncommon. Despite its rarity, severe consequences from metaldehyde poisoning have been sparingly described in earlier published reports, with doses above 100 mg/kg being associated with convulsions, and coma and death occurring at doses above 400 mg/kg.<sup>4</sup>

**Table 1.** Summary of clinical features of patients with acute toxicity from ingesting metaldehyde

Ref. no.	Pt no.	Age (years) / sex	PMHx	Cause of ingestion	Dose (g, or mg/kg)	Non-neurologic symptoms and signs	Neurologic symptoms and signs	Treatment	ICU care	LOS (days)
3	1	3.5/F	None	Accidental	NS	Nausea, vomiting, respiratory distress, cyanosis, diaphoresis, hypertension, tachycardia	Seizures, obtundation, miotic and unreactive pupils	GL, colonic irrigation, caffeine-glucose infusion, atropine, AEDs	No	2
4	2	32/F	Depression	Suicide	18.9 g, 330 mg/kg	Nausea, vomiting, elevated AG (23 mmol/L) respiratory alkalosis, rhabdomyolysis, elevated transaminases	SE, obtundation	GL, AC, AEDs	Yes	51
5	3	39/F	Depression	Suicide	12 g, 258.6 mg/kg	Flushed skin, pyrexia, diaphoresis, respiratory distress, rhabdomyolysis, elevated amylase, raised leukocytes, HAGMA (16 mmol/L), respiratory acidosis, hypotension, tachycardia	Irritability, seizures, obtundation, poorly reactive pupils	GL, AC, cathartics, i.v. NaHCO <sub>3</sub> , hemodialysis, AEDs	Yes	Death after 1 day
5	4	48/F	NS	Suicide	0.5 g	None	None	GL	No	<1
5	5	6/M	NS	Accidental	NS	None	None	GL	No	<1
5	6	5/M	NS	Accidental	1.5 g	None	None	GL	No	<1
5	7	34/M	NS	Accidental	NS	Vomiting, tachycardia	Dizziness	GL	No	<1
5	8	38/M	NS	Suicide	NS	Abdominal pain, diarrhea	None	GL	No	3
5	9	28/F	NS	Accidental	4 g	Nausea, vomiting, epistaxis	Dizziness	GL	No	3
5	10	3/M	NS	Accidental	NS	None	None	GL	No	<1
5	11	17/F	NS	Suicide	6 g	Nausea, vomiting, diarrhea	None	GL	No	<1
5	12	30/F	NS	Accidental	0.5 g	None	None	GL	No	<1
5	13	3/M	NS	Accidental	1.5 g	Oral discomfort	None	GL	No	<1
5	14	45/M	NS	Suicide	NS	Abdominal pain, vomiting, diarrhea	Headache, seizures	GL	Yes	3
5	15	6/M	NS	Accidental	2 g	None	None	GL	No	<1
5	16	5/M	NS	Accidental	2 g	None	None	GL	No	<1

Table 1. (Continued)

Ref. no.	Pt no.	Age (years) / sex	PMHx	Cause of ingestion	Dose (g, or mg/kg)	Non-neurologic symptoms and signs	Neurologic symptoms and signs	Treatment	ICU care	LOS (days)
6	17	38/M	Depression	Suicide	600 mg/kg	Vomiting, diaphoresis, tachycardia, hypotension, HAGMA (AG 48.6 mmol/L)	Seizures, obtundation, facial dystonia, fixed gaze	i.v. benzotropine 2 mg, i.v. NaHCO <sub>3</sub> ,	Yes	20
7	18	55/M	Mental retardation, pica, liver cirrhosis	Accidental	2.7 g	Respiratory distress, acute lung injury	Seizures	GL, AC, cathartic, antibiotics, pulsed steroids	Yes	Death at 33 days
5	19	37/M	Depression	Suicide	100–150 mg/kg	Pyrexia, renal impairment, hypokalemia, elevated transaminases	Comatose, recurrent seizures	GL	No	6
2	20	68/F	Depression, DM, gastric ulcers, arthritis	Suicide	NS	Mixed metabolic and respiratory acidosis, raised lactate	Refractory SE	GL, AEDs	Yes	15
9	21	46/F	Schizophrenia	Suicide	7.8 g, 150 mg/kg	HAGMA, rhabdomyolysis	Brachial plexopathy	GL, AC	No	20

Abbreviations: AC, activated charcoal; AED, antiepileptic drug; AG, anion gap; DM, diabetes mellitus; F, female; GL, gastric lavage; HAGMA, high anion-gap metabolic acidosis; ICU, intensive care unit; LOS, length of stay; M, male; NaHCO<sub>3</sub>, sodium bicarbonate; NS, not specified; PMHx, past medical history; Pt, patient; SE, status epilepticus.

**Table 2.** Comparison of patients with suicidal ingestion versus accidental ingestion of metaldehyde

	Suicidal (n = 10)	Accidental (n = 11)	P value
Age, years; median (range)	39 (17–68)	6 (3–55)	0.009
Male, n (%)	4 (40)	8 (73)	NS
Mean ingested dose, g (range) <sup>†</sup>	9.04 (0.5–18.9)	2.03 (0.5–4)	NS (0.09)
Symptomatic, n (%)	9 (90)	5 (45)	0.031
Seizures, n (%)	6 (60)	2 (18)	0.049
Require ICU care, n (%)	5 (50)	1 (9)	0.038
Death, n (%)	1 (10)	1 (9)	NS
Average LOS, days (range)	13.3 (1–51)	2.9 (1–20)	0.005

Abbreviations: ICU, intensive care unit; LOS, length of stay; NS, not significant.

<sup>†</sup>Missing data.

Metaldehyde's neurotoxic effects have been theorized to be partially caused by its aldehyde metabolites through the generation of free radicals, and also by competitively inhibiting aldehyde dehydrogenase, reducing gamma-aminobutyric acid levels within the central nervous system and consequently increasing the risks of seizures, explaining why seizures were prominent among the symptomatic patients.<sup>2,10</sup>

Our findings indicated important differences in clinical features between patients with suicidal intent and those with accidental ingestion of metaldehyde. Those with suicidal intent were twice as likely to develop symptoms of acute toxicity, three times likelier to develop seizures, five times likelier to require ICU care, with their hospitalizations being four times longer than those with accidental ingestion of metaldehyde, despite no demonstrable statistically significant differences in the metaldehyde doses due to incomplete and variable reporting in the analyzed studies. Based on these observations, the circumstances in which metaldehyde was consumed appear to significantly influence the risks of developing seizures and the patient's need for ICU care, and through these, have profound implications on the initial treatment measures and the patient's disposition (i.e., level of care), even when the dose of metaldehyde consumed was undetermined or unknown at that time. Therefore, we strongly recommend that patients with suicidal ingestion of metaldehyde must be closely monitored, especially during the earlier phases of treatment, due to their heightened risk of developing seizures. Additionally, adopting a lowered threshold when escalating their care to the ICU appears well-supported by our findings.

Our study is limited by its retrospective nature, the small number of patients, and the incomplete and inconsistent descriptions of consumed doses of metaldehyde, rendering it difficult for us to determine an association between the

ingested doses and the consequent clinical severity.<sup>4</sup> Regardless, our recommendations remain reasonable even without or before determining the ingested metaldehyde dose. These recommendations are of special practical relevance when the patients first present to an acute medical facility, as point-of-care testing for blood metaldehyde level is often unavailable, with the determination of the doses consumed being heavily dependent on the given clinical history and circumstantial evidence, a process which is often difficult and unreliable during the early phases of treatment.

## CONCLUSION AND KEY MESSAGES

THE CIRCUMSTANCES IN which metaldehyde is consumed (accidental versus suicidal consumption) heavily influence the patients' clinical symptoms and outcomes, and through these directly affect clinical decisions on treatment measures and disposition during the early stages of treatment. The risk of seizures in patients attempting suicide and their subsequent need for ICU care were increased threefold and fivefold, respectively, when compared against patients with accidental consumption of metaldehyde, despite no demonstrable statistically significant differences in the doses ingested. Therefore, it appears reasonable to base initial clinical decisions regarding the patient's initial management and disposition primarily on the circumstances in which metaldehyde was consumed. We thus recommend closely observing those who ingested metaldehyde while attempting suicide for seizures during the earlier phases of treatment, and encourage a lowered threshold when escalating their care to the ICU, even when the dose of ingested metaldehyde was unknown or undetermined at that point in time, which is a common occurrence when the patients first present.

## ACKNOWLEDGMENTS

NONE.

## DISCLOSURE

APPROVAL OF THE research protocol with approval no. and committee name: Institutional review board approval was not required due to the retrospective nature of this study.

Informed consent: N/A.

Registry and registration number of study/trial: N/A.

Animal studies: N/A.

Conflict of interest: None.

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